REMARKS

Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

I. CLAIM STATUS & AMENDMENTS

Claims 1-3, 5-8, 10-14 and 23-38 were pending in this application when last examined and stand rejected.

Claims 1 and 23 are amended. Support for these amendments can be found on page 6, lines 18-21, of the specification as filed.

No new matter has been added.

II. OBVIOUSNESS REJECTIONS

On page 2 of the Office Action, claims 1-3, 5-8, 10, 12-14 and 35-36 were rejected under 35 U.S.C. § 103 as unpatentable over Anderson (U.S. 2004/0028772) in view of Cherukuri et al. (U.S. 4,238,510). On page 4, claim 11 was rejected under 35 U.S.C. § 103 as unpatentable over the above two references in view of Hill (U.S. 5,380,530). At the bottom of page 4, claims 23-30 and 32-34 were rejected under 35 U.S.C. § 103 as unpatentable over Johnson et al. (U.S. 6,627,234). On page 6, claim 31 was rejected under 35 U.S.C. § 103 as unpatentable over Johnson et al. in view of Hill. Lastly, claims 37-38 were rejected under 35 U.S.C. § 103 as unpatentable over Johnson et al. in view of Kurihara et al. (U.S. 5,344,659). Applicants respectfully traverse these rejections, as applied to the amended claims, for the following reasons.

Applicants note that claims 1 and 23 are amended to require the inclusion of mannitol, sorbitol or xylitol in the second formulation in an amount sufficient to improve the palatability of the pharmaceutical composition. Applicants note that the Examiner contends that the inclusion of mannitol in the claimed formulations is obvious in light of Anderson, Cherukuri et al. or Johnson et al. Applicants respectfully disagree.

In particular, these three references only provide general guidance to a person of skill in the art investigating medicaments with compounds of claimed formula I. A skilled artisan may look to such references to ascertain lists of acceptable components for

the claimed pharmaceutical. However, a skilled artisan would also examine references that describe medicaments with compounds of formula I for more particular guidance. In particular, EP 0811374, cited previously by Applicants, is particularly concerned with medicaments containing cetirizine, a compound of formula I.

However, EP 0811374 teaches that low molecular weight alcohols adversely effects stability of compounds of formula I. In particular, EP 0811374 indicates the following:

> 1) In a preferred embodiment, the dosage form is substantially free of alcohols having a molecular weight less than 250, and reactive derivatives thereof. In a more preferred embodiment, the dosage form is substantially free of alcohols having a molecular weight less than 500 and reactive derivatives thereof. In a still more preferred embodiment, the dosage form is substantially free of alcohols having a molecular weight less than 1000 and reactive derivatives thereof. [See page 2, line 58 to page 3, line 3 of EP 0 811 374 A1]
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> 2) The fact that alcohols and derivatives thereof such as esters are deleterious to formulations containing cetirizine is surprising in view of the fact that esters, for example glycerol esters, of cetirizine are difficult to make by conventional direct esterification methods. In view of the difficulty associated with direct esterification, it is surprising that cetirizine reactivity towards alcohols is such that extensive ester formation was observed when using processes to make dry solid formulations, such as tablets, in which cetirizine was exposed to glycerin or other alcohols in one or more steps. [See page 5, lines 29-33 of EP 0 811 374 A1]
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> 3) Thus the final dosage form, in both the core and outside layer(s), must be substantially free of low molecular weight alcohols and reactive derivatives thereof. Such materials include relatively low molecular weight monohydric and polyhydric alcohols which are conventionally known and frequently, if not universally, used as solvents in the formulations arts, and compositions containing them as vehicles or carriers. Examples of such reactive alcohols include lower molecular weight alcohols such as methanol, ethanol, isopropanol, and glycerin. Because they are difficult to remove, high boiling point alcohols such as glycerin can be problematic, and it is preferred such components be avoided altogether. Many plasticizers are alcohols, and contact with cetirizine should accordingly be avoided as well if they have a low molecular weight. Many plasticizers are also esters, i.e., materials which are reactive derivatives of alcohols, and contact of cetirizine with these materials should be avoided as well since the ester groups can undergo transesterification with cetirizine and thereby damage the dosage form. [See page 4, lines 3-12 of EP 0 811 374 A1]

Thus, this reference teaches (1) preferred embodiments of the cetirizine medicament are substantially free of alcohols with molecular weights less than 250; (2) cetirizine reacts with alcohols presence in the formulation by esterification; and (3) the entire formulation (which can be composed of two separate layers) should be free of low molecular weight alcohols.

Applicants note that this reference defines polyols as alcohols. Applicants further note that this reference particularly indicates that alcohols less than 100 MW should be

avoided. However, a person of skill in the art reading this reference would understand that such a molecular weight cut-off was utilized because the authors were particularly concerned with low molecular weight alcohols used for processing the disclosed formulations. Further, a skilled artisan would understand based on this reference that low molecular weight alcohols, such as mannitol, sorbitol or xylitol, would degrade cetirizine. In fact, Example 2 of this reference, which is a preferred embodiment, has no alcohols present in the final formulation except for a 3350 MW polyethylene glycol.

Therefore, this reference teaches away from adding mannitol, sorbitol or xylitol in an amount sufficient to improve palatability to a medicament containing a compound of formula I because it teaches that such low molecular weight polyols would degrade compounds of formula I by esterification.

Thus, a person of skill in the art would be dissuaded from using mannitol, sorbitol or xylitol as a palatability improving component of the claimed formulation based on the generalized teachings of Anderson, Cherukuri et al. or Johnson et al. because of the particular teachings of EP 0811374 regarding cetirizine formulations.

For the above noted reasons, Applicants submit that a person of skill in the art would not be motivated to either combine the cited references or "pick and choose" optional elements of the cited references to arrive at the invention of the amended claims. Therefore, Applicants respectfully suggest that these rejections, as applied to the amended claims, should be withdrawn as untenable.

CONCLUSION

In view of the foregoing amendments and remarks, it is respectfully submitted that the present application is in condition for allowance and early notice to that effect is hereby requested.

If the Examiner has any comments or proposals for expediting prosecution, please contact the undersigned attorney at the telephone number below.

Respectfully submitted,

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